

## Supporting Information

### Synthetic Utility of an Isolable Nucleoside Phosphonium Salt

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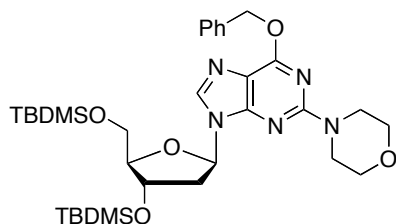
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## GENERAL EXPERIMENTAL METHODS

Reactions were monitored by TLC (silica gel, 250  $\mu\text{m}$ ), and column chromatographic purifications were performed on 200–300 mesh silica gel. Solvents used for eluting the compounds, as well as TLC conditions and  $R_f$  values, are provided under individual compound headings.  $\text{CH}_2\text{Cl}_2$  and (*iso*-Pr) $_2\text{NEt}$  were distilled over  $\text{CaH}_2$ . All other reagents were obtained from commercial sources and were used without further purification.  $^1\text{H}$  NMR spectra were recorded at 500 MHz and were referenced to the residual protonated solvent.  $^{13}\text{C}$  NMR spectra were recorded at 125 MHz and were referenced to  $\text{CDCl}_3$ .  $^{31}\text{P}\{^1\text{H}\}$  NMR spectra were recorded at 202 MHz and were referenced to 85%  $\text{H}_3\text{PO}_4$  as an external standard. Chemical shifts are reported in parts per million ( $\delta$ ), and coupling constants ( $J$ ) are in hertz. The sugar protons are numbered 1'–5' beginning at the anomeric carbon and proceeding via the carbon chain to the primary carbinol carbon. All HRMS samples were analyzed by positive ion ESI.

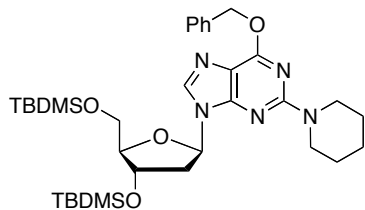
### *O*<sup>6</sup>-Benzyl-3',5'-bis-*O*-(*tert*-butyldimethylsilyl)-2-(morpholin-4-yl)-2'-deoxyinosine (**4a**).



To a solution of the nucleoside phosphonium salt **3** (49.5 mg, 0.055 mmol) in dry DME (0.5 mL) was added morpholine (19.4  $\mu\text{L}$ , 0.222 mmol). The reaction vial was flushed with nitrogen gas and the mixture was allowed to stir at room temperature for 26 h. The reaction mixture was directly loaded onto a bed of  $\text{SiO}_2$  and the product was eluted using EtOAc to give 32.6 mg (90% yield) of compound **4a** as a clear gum.  $R_f$  (20% EtOAc in hexanes) = 0.21.  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.87 (s, 1H, H-8), 7.48 (d, 2H, Ar-H,  $J = 7.5$ ), 7.33 (t, 2H, Ar-H), 7.28 (t, 1H, Ar-H,  $J = 7.3$ ), 6.32 (t, 1H, H-1',  $J = 6.6$ ), 5.55 (AB<sub>quart</sub>, 2H, OCH<sub>2</sub>,  $J = 12.2$ ), 4.58 (quint, 1H, H-3',  $J = 3.1$ ), 3.96 (q, 1H, H-4',  $J = 3.7$ ), 3.80–3.75 (m, 10H, H-5' and morpholinyl CH<sub>2</sub>), 2.64 (app quint, 1H, H-2',  $J \sim 6.5$ ), 2.31 (ddd, 1H, H-2',  $J = 12.9, 6.1, 3.7$ ), 0.914, 0.91 (2s, 18H, *t*-Bu), 0.10, 0.074, 0.07 (3s, 12H, SiCH<sub>3</sub>).  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  160.2, 158.4, 153.7, 138.0, 136.8, 128.3, 128.0, 127.9, 115.2, 87.6, 83.8, 72.1, 67.8, 66.8, 63.0, 45.0, 40.6, 26.0, 25.8, 18.4, 18.0, -4.7, -4.8, -5.4, -5.5.

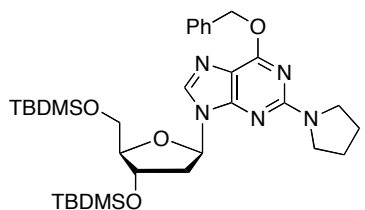
### *O*<sup>6</sup>-Benzyl-3',5'-bis-*O*-(*tert*-butyldimethylsilyl)-2-(piperidin-1-yl)-2'-deoxyinosine (**4b**).

As described for the synthesis of **4a**, piperidinyl derivative **4b** was prepared by reaction of nucleoside phosphonium salt **3** (69.2 mg, 0.077 mmol) and piperidine (30.6  $\mu\text{L}$ , 0.310 mmol) in



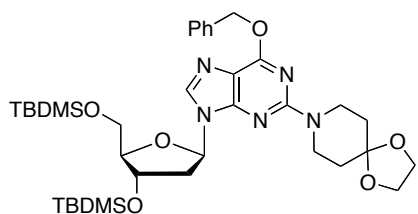
dry DME (0.8 mL) at room temperature over 23 h. The reaction mixture was directly loaded onto a bed of SiO<sub>2</sub> and the product was eluted using EtOAc to give 48.6 mg (96% yield) of compound **4b** as a yellow gum.  $R_f$  (20% EtOAc in hexanes) = 0.22. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ 7.79 (s, 1H, H-8), 7.32 (d, 2H, Ar-H,  $J$  = 7.3), 7.33 (t, 2H, Ar-H,  $J$  = 7.3), 7.27 (m, 1H, Ar-H), 6.30 (t, 1H, H-1',  $J$  = 6.6), 5.55 (AB<sub>quart</sub>, 2H, OCH<sub>2</sub>,  $J$  = 12.5), 4.58 (app quint, 1H, H-3',  $J$  ~ 3.1), 3.95 (q, 1H, H-4',  $J$  = 3.8), 3.81–3.74 (m, 6H, H-5' and piperidiny CH<sub>2</sub>), 2.68 (app quint, 1H, H-2',  $J$  ~ 6.5), 2.31 (ddd, 1H, H-2',  $J$  = 12.5, 6.1, 3.7), 1.67–1.64 (br m, 2H, piperidiny CH<sub>2</sub>), 1.60–1.56 (br m, 4H, piperidiny CH<sub>2</sub>), 0.92, 0.90 (2s, 18H, *t*-Bu), 0.10, 0.07, 0.066 (3s, 12H, SiCH<sub>3</sub>). <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ 160.1, 158.5, 153.9, 137.6, 137.1, 128.2, 128.1, 127.7, 114.6, 87.5, 83.8, 72.2, 67.5, 63.1, 45.6, 40.4, 26.0, 25.74, 25.7, 24.9, 18.4, 18.0, -4.7, -4.8, -5.4, -5.5.

***O*<sup>6</sup>-Benzyl-3',5'-bis-*O*-(*tert*-butyldimethylsilyl)-2-(pyrrolidin-1-yl)-2'-deoxyinosine (**4c**).**



As described for the synthesis of **4a**, pyrrolidiny derivative **4c** was prepared by a reaction between nucleoside phosphonium salt **3** (69.7 mg, 0.078 mmol) and pyrrolidine (26.0 μL, 0.312 mmol) in dry DME (0.8 mL) at room temperature over 23 h. The reaction mixture was directly loaded onto a bed of SiO<sub>2</sub> and the product was eluted using EtOAc to give 50.0 mg (quantitative yield) of compound **4c** as a clear gum.  $R_f$  (20% EtOAc in hexanes) = 0.24. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ 7.74 (s, 1H, H-8), 7.51 (d, 1H, Ar-H,  $J$  = 7.3), 7.33 (t, 2H, Ar-H,  $J$  = 7.5), 7.28–7.26 (m, 1H, Ar-H), 6.28 (t, 1H, H-1',  $J$  = 6.7), 5.58 (AB<sub>quart</sub>, 2H, OCH<sub>2</sub>,  $J$  = 12.4), 4.59 (quint, 1H, H-3',  $J$  = 2.9), 3.96 (m, 1H, H-4'), 3.83 (dd, 1H, H-5',  $J$  = 11.0, 5.9), 3.76 (dd, 1H, H-5',  $J$  = 11.0, 3.8), 3.58 (br t, 4H, pyrrolidiny NCH<sub>2</sub>,  $J$  ~ 6.4), 2.79 (app quint, 1H, H-2',  $J$  ~ 6.6), 2.27 (ddd, 1H, H-2',  $J$  = 13.1, 6.1, 3.4), 1.98–1.95 (m, 4H, pyrrolidiny CH<sub>2</sub>), 0.92, 0.90 (2s, 18H, *t*-Bu), 0.10, 0.07, 0.06 (3s, 12H, SiCH<sub>3</sub>). <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ 160.1, 157.2, 153.9, 137.3, 137.2, 128.2, 128.19, 127.7, 114.6, 87.6, 84.2, 72.4, 67.4, 63.2, 47.0, 25.9, 25.7, 25.5, 18.4, 18.0, -4.7, -4.8, -5.4, -5.45.

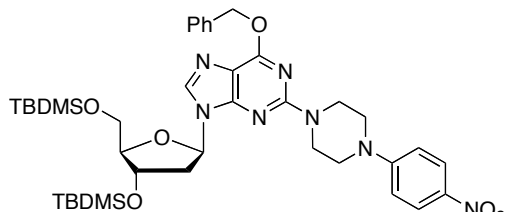
***O*<sup>6</sup>-Benzyl-3',5'-bis-*O*-(*tert*-butyldimethylsilyl)-2-(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)-2'-deoxyinosine (**4d**).**



As described for the synthesis of **4a**, azaspirodecyl derivative **4d** was prepared by a reaction between nucleoside phosphonium salt **3** (87.1 mg, 0.097 mmol) and 1,4-dioxaspiro[4.5]decane (50.0  $\mu$ L, 0.390 mmol) in dry DME (1.0 mL) at room temperature for 23 h and then at 85  $^{\circ}$ C for 1 h.

The reaction mixture was directly loaded onto a bed of SiO<sub>2</sub> and the product was eluted using EtOAc to give 57.4 mg (83% yield) of **4d** as a yellow gum.  $R_f$  (20% EtOAc in hexanes) = 0.16. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>):  $\delta$  7.83 (s, 1H, H-8), 7.48 (d, 2H, Ar-H,  $J$  = 7.0), 7.32 (app t, 2H, Ar-H,  $J$   $\sim$  7.2), 7.29–7.26 (m, 1H, Ar-H), 6.31 (t, 1H, H-1',  $J$  = 6.7), 5.55 (AB<sub>quart</sub>, 2H, OCH<sub>2</sub>Ph,  $J$  = 12.2), 4.57 (app quint, 1H H-3',  $J$   $\sim$  3.1), 4.01 (s, 4H, OCH<sub>2</sub>), 3.96 (app q, 1H, H-4',  $J$   $\sim$  3.8), 3.92 (br t, 4H, NCH<sub>2</sub>,  $J$   $\sim$  5.6), 3.80–3.74 (m, 2H, H-5'), 2.62 (app quint, 1H, H-2',  $J$   $\sim$  6.5), 2.32 (ddd, 1H, H-2',  $J$  = 13.1, 6.1, 3.7), 1.71 (br t, 4H, CH<sub>2</sub>,  $J$   $\sim$  5.8), 0.91, 0.905 (2s, 18H, *t*-Bu), 0.10, 0.07 (2s, 12H, SiCH<sub>3</sub>). <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>):  $\delta$  160.1, 158.0, 153.9, 137.6, 137.0, 128.2, 128.0, 127.7, 114.7, 107.7, 87.5, 83.7, 72.1, 67.7, 64.3, 63.0, 42.7, 40.6, 34.6, 25.9, 25.7, 18.4, 17.9, -4.7, -4.8, -5.4, -5.5.

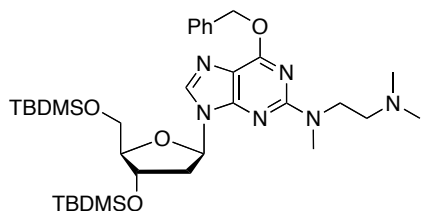
***O*<sup>6</sup>-Benzyl-3',5'-bis-*O*-(*tert*-butyldimethylsilyl)-2-[4-(4-nitrophenyl)-piperizin-1-yl]-2'-deoxyinosine (**4e**).**



As described for the synthesis of **4a**, 4-nitrophenyl piperazine derivative **4e** was prepared by a reaction between nucleoside phosphonium salt **3** (85.9 mg, 0.096 mmol) and 1-(4-nitrophenyl)piperazine (79.6 mg, 0.384 mmol) in dry DME (1.0 mL) at room temperature for 23 h and then at 85  $^{\circ}$ C for 3 h. The reaction mixture was evaporated to dryness and chromatographic purification (SiO<sub>2</sub>, 50% EtOAc in hexanes) afforded 48.6 mg (65% yield) of compound **4e** as a yellow solid.  $R_f$  (5% MeOH in CH<sub>2</sub>Cl<sub>2</sub>) = 0.79. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>):  $\delta$  8.16 (d, 2H, Ar-H,  $J$  = 9.5), 7.91 (s, 1H, H-8), 7.49 (d, 2H, Ar-H,  $J$  = 7.3), 7.35 (app t, 2H, Ar-H,  $J$   $\sim$  7.5), 7.30 (t, 1H, Ar-H,  $J$  = 7.5), 6.85 (d, 2H, Ar-H,  $J$  = 9.5), 6.36 (t, 1H, H-1',  $J$  = 6.7), 5.59 (AB<sub>quart</sub>, 2H, OCH<sub>2</sub>,  $J$  = 12.4), 4.59 (br app quint, 1H, H-3',  $J$   $\sim$  3.0), 4.00–3.98 (br m, 4H, NCH<sub>2</sub>), 3.82–3.76 (m, 2H, H-5'), 3.51 (br t, 4H, NCH<sub>2</sub>,  $J$  = 5.2), 2.59 (app quint, 1H, H-2',  $J$   $\sim$  6.5), 2.34 (ddd, 1H, H-2',  $J$  = 13.1, 5.8, 3.7), 0.93, 0.92 (2s, 18H, *t*-Bu), 0.12, 0.09

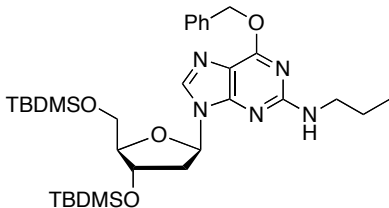
(2s, 12H, SiCH<sub>3</sub>). <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ 160.2, 158.0, 154.7, 153.8, 138.5, 137.9, 136.8, 128.3, 127.9, 127.8, 125.9, 115.2, 112.5, 87.6, 83.6, 72.1, 67.9, 63.0, 46.7, 43.8, 40.9, 25.9, 25.7, 18.4, 18.0, -4.7, -4.8, -5.4, -5.5.

***O*<sup>6</sup>-Benzyl-3',5'-bis-*O*-(*tert*-butyldimethylsilyl)-*N*<sup>2</sup>-methyl-*N*'-[(2-*N,N*-dimethylamino)ethyl]-2'-deoxyguanosine (**4f**).**



As described for the synthesis of **4a**, trimethylethylenediamine derivative **4f** was prepared by a reaction between nucleoside phosphonium salt **3** (81.5 mg, 0.091 mmol) and *N,N,N'*-trimethylethylenediamine (47.4 μL, 0.365 mmol) in dry DME (1.0 mL) at room temperature for 23 h and then at 85 °C for 3 h. The reaction mixture was evaporated to dryness and chromatographic purification (SiO<sub>2</sub>, 5% MeOH in EtOAc) afforded 43.3 mg (71% yield) of compound **4f** as a yellow foam. *R<sub>f</sub>* (5% MeOH in CH<sub>2</sub>Cl<sub>2</sub>) = 0.20. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ 7.81 (s, 1H, H-8), 7.47 (d, 2H, Ar-H, *J* = 7.3), 7.33 (t, 2H, Ar-H, *J* ~ 7.3), 7.29–7.26 (m, 1H, Ar-H), 6.31 (t, 1H, H-1', *J* = 6.6), 5.56 (AB<sub>quart</sub>, 2H, PhCH<sub>2</sub>O, *J* = 12.2), 4.55 (br app quint, 1H, H-3', *J* ~ 2.8), 3.96 (app q, 1H, H-4', *J* ~ 3.7), 3.80–3.72 (m, 4H, H-5' and NCH<sub>2</sub>), 3.18 (s, 3H, NCH<sub>3</sub>), 2.66–2.58 (m, 3H, H-2' and NCH<sub>2</sub>), 2.34 (s, 6H, NCH<sub>3</sub>), 2.34–2.29 (m, 1H, H-2'), 0.91, 0.90 (2s, 18H, *t*-Bu), 0.10, 0.07 (2s, 12H, SiCH<sub>3</sub>). <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ 160.0, 158.5, 153.9, 137.2, 136.9, 128.3, 127.9, 127.8, 114.3, 87.6, 83.8, 72.2, 67.5, 63.1, 56.8, 47.7, 45.6, 40.6, 36.1, 25.9, 25.7, 18.4, 17.9, -4.7, -4.8, -5.4, -5.5.

***O*<sup>6</sup>-Benzyl-3',5'-bis-*O*-(*tert*-butyldimethylsilyl)-*N*<sup>2</sup>-propyl-2'-deoxyguanosine (**4g**).**



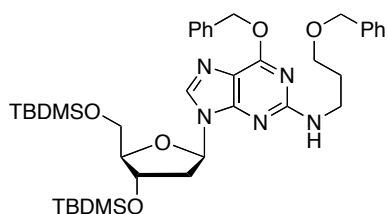
To a solution of nucleoside phosphonium salt **3** (77.7 mg, 0.087 mmol) in dry DME (0.9 mL) was added *n*-propylamine (28.6 μL, 0.348 mmol). The reaction vial was flushed with nitrogen gas and the mixture was allowed to stir at room temperature for 23 h then at 85 °C for 3 h. TLC indicated that the reaction was incomplete and therefore, additional *n*-propylamine (25.0 μL, 0.304 mmol) was added to the mixture. The reaction was allowed to continue at 85 °C and was complete within 5 h. The reaction mixture was directly loaded onto a bed of SiO<sub>2</sub> and the product was eluted with EtOAc to give 37.2 mg (68% yield) of compound **4g** as a clear gum. *R<sub>f</sub>* (5% MeOH in CH<sub>2</sub>Cl<sub>2</sub>)

= 0.86.  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.82 (s, 1H, H-8), 7.49 (d, 2H, Ar-H,  $J = 7.3$ ), 7.34 (app t, 2H, Ar-H,  $J \sim 7.3$ ), 7.28–7.26 (m, 1H, Ar-H), 6.30 (t, 1H, H-1',  $J = 6.6$ ), 5.55 (AB<sub>quart</sub>, 2H, OCH<sub>2</sub>,  $J = 12.5$ ), 4.92 (br t, 1H, NH,  $J = 5.5$ ), 4.58 (app quint, 1H, H-3',  $J \sim 3.0$ ), 3.97 (br app q, 1H, H-4',  $J \sim 3.7$ ), 3.80 (dd, 1H, H-5',  $J = 11.0, 4.7$ ), 3.76 (dd, 1H, H-5',  $J = 11.0, 3.7$ ), 3.38 (app q, 2H, NCH<sub>2</sub>,  $J \sim 6.6$ ), 2.63 (app quint, 1H, H-2',  $J \sim 6.5$ ), 2.32 (ddd, 1H, H-2',  $J = 13.1, 6.1, 3.7$ ), 1.62 (q, 2H, CH<sub>2</sub>,  $J = 7.2$ ), 0.98 (t, 3H, CH<sub>3</sub>,  $J = 7.5$ ), 0.92, 0.91 (2s, 18H, *t*-Bu), 0.10, 0.073, 0.07 (3s, 12H, SiCH<sub>3</sub>).  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  160.6, 159.1, 153.9, 137.2, 136.9, 128.3, 128.2, 127.8, 115.3, 87.6, 83.8, 72.2, 67.6, 63.0, 43.8, 40.6, 26.0, 25.7, 22.9, 18.4, 18.0, 11.5, -4.7, -4.8, -5.4, -5.5.

### General procedure for the debenzoylation of $N^2$ -modified derivatives 4a-d, f, g.

To a solution of  $N^2$ -modified derivatives **4** (34.6–49.7 mg) in 1:1 THF–MeOH (3.0 mL) was added 10% Pd-C (4.0–5.0 mg). The flask was evacuated and filled with hydrogen gas, and this procedure was repeated three times. The mixture was then stirred under 1 atm of hydrogen gas (balloon) at room temperature until the reaction was complete (usually about 4 h). The reaction mixture was filtered through a plug of Celite, the residue was washed with MeOH and the filtrate was evaporated to dryness. No additional purification was needed for compounds **5a**, **5b**, **5d** and **5g**. Compound **5c** was chromatographed on SiO<sub>2</sub> using 5% MeOH in CH<sub>2</sub>Cl<sub>2</sub> and compound **5f** was chromatographed on SiO<sub>2</sub> using 10% MeOH in CH<sub>2</sub>Cl<sub>2</sub>. Characterization data for **5a-d**, **f**, **g** have been reported previously (reference 4a in the paper).

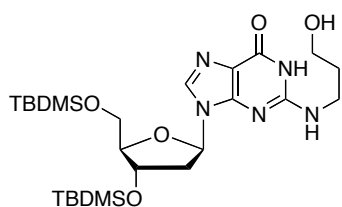
### $O^6$ -Benzyl- $N^2$ -(3-benzyloxy-1-propyl)-3',5'-bis- $O$ -(*tert*-butyldimethylsilyl)-2'-deoxyguanosine (**7**).



To a solution of nucleoside phosphonium salt **3** (113.7 mg, 0.127 mmol) in dry DME (1.5 mL) was added 3-benzyloxypropylamine (87% purity, 125.9 mg, 0.663 mmol). The reaction mixture was flushed with nitrogen gas and allowed to stir at 85 °C for 3 h, and then evaporated to dryness. Chromatographic purification (SiO<sub>2</sub>, 20% EtOAc in hexanes) afforded 76.7 mg (82% yield) of compound **7** as a clear gum.  $R_f$  (20% EtOAc in hexanes) = 0.18.  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.83 (s, 1H, H-8), 7.48 (d, 2H, H-8,  $J = 7.3$ ), 7.37–7.28 (m, 8H, Ar-H), 6.31 (t, 1H, H-1',  $J = 6.6$ ), 5.53 (AB<sub>quart</sub>, 2H, OCH<sub>2</sub>,  $J = 12.4$ ), 5.20 (br, 1H, NH, D<sub>2</sub>O exchangeable), 4.57 (m, 1H, H-3'), 4.53 (s, 2H, OCH<sub>2</sub>), 3.96 (br app q, 1H,

H-4',  $J \sim 3.4$ ), 3.80 (dd, 1H, H-5',  $J = 11.0, 4.6$ ), 3.76 (dd, 1H, H-5',  $J = 11.0, 3.4$ ), 3.60 (t, 2H, CH<sub>2</sub>O,  $J = 5.8$ ), 3.57–3.53 (m, 2H, NCH<sub>2</sub>), 2.60 (app quint, 1H, H-2',  $J = 6.4$ ), 2.32 (ddd, 1H, H-2',  $J = 13.0, 5.9, 3.7$ ), 1.92 (app quint, 2H, CH<sub>2</sub>,  $J = 6.0$ ), 0.913, 0.91 (2s, 18H, *t*-Bu), 0.10, 0.07 (2s, 12H, SiCH<sub>3</sub>). <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>):  $\delta$  160.5, 159.0, 153.8, 138.3, 137.2, 136.8, 128.3, 128.2, 128.1, 127.6, 127.5, 115.3, 87.5, 83.6, 73.0, 72.0, 68.6, 67.6, 62.9, 40.7, 39.8, 29.5, 25.9, 25.7, 18.4, 17.9, -4.7, -4.8, -5.4, -5.5. ESI HRMS calcd for C<sub>39</sub>H<sub>59</sub>N<sub>5</sub>O<sub>5</sub>Si<sub>2</sub>Na (M<sup>+</sup> + Na) 756.3947, found 756.3940.

**3',5'-Bis-*O*-(*tert*-butyldimethylsilyl)-*N*<sup>2</sup>-(3-hydroxy-1-propyl)-2'-deoxyguanosine (8).**

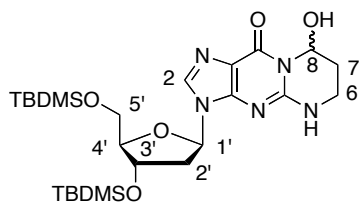


To a solution of dibenzyl-protected nucleoside **7** (120.4 mg, 0.164 mmol) in 1:1 THF–MeOH (12 mL) was added 10% Pd-C (30 mg). The flask was evacuated and filled with hydrogen gas, and this procedure was repeated three times. The mixture was then stirred under 1 atm of hydrogen gas (balloon) at room temperature for 23

h. Upon completion of the reaction, the mixture was filtered through a plug of Celite, the residue was washed with MeOH and the filtrate was evaporated to dryness. Chromatographic purification (SiO<sub>2</sub>, 10% MeOH in CH<sub>2</sub>Cl<sub>2</sub>) afforded 81.2 mg (89% yield) of compound **8** as a white solid.  $R_f$  (5% MeOH in CH<sub>2</sub>Cl<sub>2</sub>) = 0.04. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>):  $\delta$  10.90 (br s, 1H, NH, D<sub>2</sub>O exchangeable), 7.77 (s, 1H, H-8), 6.26 (t, 1H, H-1',  $J = 6.5$ ), 6.04 (br, 1H, OH, D<sub>2</sub>O exchangeable), 4.57 (m, 1H, H-3'), 3.97 (br q, 1H, H-4',  $J \sim 3.7$ ), 3.83 (br, 2H, CH<sub>2</sub>OH), 3.81–3.76 (m, 2H, H-5'), 3.72–3.65 (m, 2H, NHCH<sub>2</sub>), 2.56 (app quint, 1H, H-2',  $J = 6.4$ ), 2.37 (ddd, 1H, H-2',  $J = 13.1, 6.1, 4.3$ ), 1.85–1.81 (br m, 2H, CH<sub>2</sub>), 0.92, 0.91 (2s, 18H, *t*-Bu), 0.11, 0.09 (2s, 12H, SiCH<sub>3</sub>). The NH proton appears at 7.77 (overlaps with H-8 and is D<sub>2</sub>O exchangeable). Upon exchange with D<sub>2</sub>O signal at 3.82 (br t, 2H, CH<sub>2</sub>OH,  $J \sim 5.6$ ). <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>):  $\delta$  158.4, 153.1, 151.8, 135.9, 116.3, 87.7, 84.0, 71.9, 62.9, 58.3, 40.9, 37.6, 31.0, 25.9, 25.7, 18.4, 18.0, -4.7, -4.8, -5.4, -5.5. ESI HRMS calcd for C<sub>25</sub>H<sub>47</sub>N<sub>5</sub>O<sub>5</sub>Si<sub>2</sub>Na (M<sup>+</sup> + Na) 576.3008, found 576.2997.

**The ~1:1 diastereomeric mixture of 3-[3,5-bis-*O*-(*tert*-butyldimethylsilyl)-2-deoxy- $\beta$ -D-ribofuranosyl]-8-hydroxy-5,6,7,8-tetrahydropyrimido[1,2-*a*]purin-10(3*H*)-one (9).**

In a clean, dry vial equipped with a stirring bar were placed 3-hydroxy-1-propyl 2'-deoxyguanosine derivative (**8**) (40.8 mg, 0.074 mmol), 4-acetylamino-2,2,6,6-



tetramethylpiperidine-1-oxoammonium tetrafluoroborate (26.5 mg, 0.088 mmol) and silica gel (123 mg). Dry  $\text{CH}_2\text{Cl}_2$  (4.0 mL) was added, the mixture was flushed with nitrogen gas, and then allowed to stir at room temperature for 13 h. Upon completion, the reaction mixture was concentrated and subjected to chromatographic purification ( $\text{SiO}_2$ , eluted with 20% acetone in hexanes and then 5% MeOH in  $\text{CH}_2\text{Cl}_2$ ) to afford 28.0 mg (69% yield) of compound **9** as a white, foamy solid.  $R_f$  (5% MeOH in  $\text{CH}_2\text{Cl}_2$ ) = 0.08.  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.76 and 7.75 (2s, 1H each, H-2 of each diastereomer), 6.26 (br, 1H, H-8), 6.19 (t, 1H, H-1',  $J = 6.6$ ), 5.51 (br s, 1H, NH,  $\text{D}_2\text{O}$  exchangeable), 4.55 (m, 1H, H-3'), 4.36 (br m, 1H, 8-OH,  $\text{D}_2\text{O}$  exchangeable), 3.96 (q, 1H, H-3',  $J = 3.5$ ), 3.78–3.72 (m, 2H, H-5'), 3.64 (app td, 1H, H-6a,  $J \sim 12.4, 3.0$ ), 3.39 (m, 1H, H-6b), 2.49–2.42 (m, 1H, H-2'), 2.33–2.28 (overlapping of ddd and m, 2H, H-2' and H-7a,  $J = 12.9, 6.1, 3.4$ ), 1.94 (br tm, 1H, H-7b,  $J \sim 13.0$ ), 0.91, 0.906 (2s, 18H, *t*-Bu), 0.10, 0.074, 0.07 (3s, 12H,  $\text{SiCH}_3$ ).  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  157.5, 150.9 and 150.8 (2s), 149.8, 135.5 and 135.4 (2s), 116.7, 87.6, 83.1 and 83.0 (2s), 71.9 and 71.85 (2s), 71.8, 62.8, 41.0, 34.3, 27.1, 27.09 and 27.04 (2s), 25.9, 25.7, 18.4, 18.0, -4.7, -4.8, -5.4, -5.5. ESI HRMS calcd for  $\text{C}_{25}\text{H}_{45}\text{N}_5\text{O}_5\text{Si}_2\text{Na}$  ( $\text{M}^+ + \text{Na}$ ) 574.2851, found 574.2841.